Nitrosation of Benzoxazolinone

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2(3)-benzoxazolinone (**I**) has been isolated from rye (Virtanen and Hietala, 1955), corn, and wheat (Virtanen, *et al.*, 1956). It was later found that this compound is stored in the plant as the glucoside of 1,4-benzoxzinone and is formed when the plant is injured. Klun and Robinson (1969) found concentrations as high as 1.4 mg/g in inbred strains of corn and had shown that the presence of the compound was associated with the resistance of the plant to attack by fungi and corn borer.

A wide variety of N-nitroso amines, amides, ureas, and carbamates have been shown to be extremely potent carcinogens and their presence in food products has been of considerable public health concern (Magee and Barnes, 1967; Low, 1974). Since these compounds are readily formed by the action of nitrite ion on the appropriate precursor under acidic conditions, it was felt that N-nitrosobenzoxazolinone (**II**) might be formed in corn, wheat, or rye that had been heavily fertilized with nitrite-nitrate or that the nitroso compound may be formed through the action of dietary nitrite.

In an attempt to form **II**, 0.01 mole of **I**, 0.02 mole $NaNO_2$, and 0.02 mole HCl were stirred at 0° for 12 hr. in an aqueous medium. However, the starting material was recovered nearly quantitatively. The procedure was repeated using glacial acetic acid as the solvent and proton source (10°, 26 hr.), and again only starting material was found. In a third attempt, trifluoroacetic acid was used as the solvent and proton source (0°, 22 hr.), and the reaction mixture was found to contain a small quantity of **I** and a nearly quantitative yield of 6-nitrobenzoxazolinone (**III**). The identity of **III** was confirmed by TLC, IR, and mass spectral data of an authentic standard. Activated aromatic systems, such as with phenols, usually yield C-nitroso compounds with nitrous acid which are then oxidized to C-nitro compounds. Since **III** is easily formed from **I** by the action of nitric acid at room temperature (Clark and Pessolona, 1958), the formation of the N-nitroso derivative in this case probably occurs in a similar manner.

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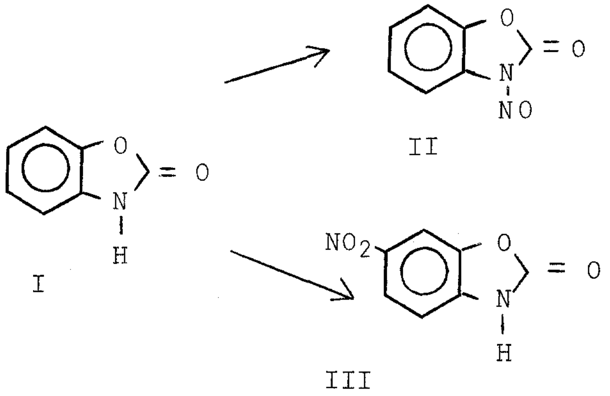

Nitrogen tetroxide has been successfully used in the preparation of N-nitroso amides that could not be successfully prepared with $NaNO_2$ (White, 1955). In this case, 0.01 mole I was dissolved in 50 ml methylene chloride, 0.03 mole of anhydrous sodium acetate was added, the mixture was cooled to -70°, then 0.02 mole of nitrogen tetroxide was added. The mixture was brought to 0°, then after 1 hr. it was washed with 30 ml of a 5% $NaHCO_3$ solution. The methylene chloride layer was dried and the solvent was removed under vacuum at 0°. The residue was found to be primarily III with a small amount of starting material.

Nitrosyl chloride with glacial acetic acid, potassium acetate, and phosphorous pentoxide has been used by Ahmed and Hay (1959) to prepare 1-methoxy-2-N-nitrosoacetamidonaphthalene. When this procedure was used for the preparation of II, the product was found to contain mostly N-acetylbenzoxazolinone and small quantities of III and N-acetyl-6-nitrobenzoxazolinone. In order to avoid acetylation, the procedure was repeated using 0.01 mole I, 0.03 mole nitrosyl chloride, and 0.05 mole pyridine at 0° in dimethoxyethane. After 1 hr., the reaction mixture was found to contain mostly I and III in addition to a very small quantity of a third component that could not be identified.

Several attempts were also made a preparing 6-nitro-N-nitroso-benzoxazolinone from III. A suspension of III, $NaNO_2$, and HCl was stirred under nitrogen at 0°. After 49 hrs., nearly 100% of the starting material was recovered. Attempts at the nitrosation using nitrogen tetroxide and nitrosyl chloride also failed.

Though N-aryl amides are most difficult to nitrosate than the corresponding N-alkyl amides, the resistance of I and III to nitrosation was unexpected. Mirvish (1975) could also not produce the nitroso derivatives of the ureas diphenylhydantoin, barbital, and phenobarbital. The resistance of I and III may also be due to their cyclic nature which prevents attack by the nitrosating reagent.

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